REMARKS

Claims 1-22 are currently pending in the application. Claims 20 and 21 are canceled. Claims 1-12, 17-19, and 22 are amended herein. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Applicants wish to thank Examiner Zitomer for the telephone interview of May 7, in which the outstanding enablement and prior art rejections were discussed. The substance of that interview is incorporated into the present response and will be referred to where appropriate.

Rejection of Claims 1-22 under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 1-22 under 35 U.S.C. §112, first paragraph for lack of enablement. As discussed during Applicant's telephone interview with the Examiner, the Examiner will withdraw the rejection with respect to claims 1-16. Accordingly, Applicants following remarks pertain to claims 17-22.

The Examiner asserts that the specification, "while being enabled for *in vitro* methods of use, does not reasonably provided enablement for *in vivo* methods". The Examiner asserts that at the time the application was filed, the prior art taught that gene therapy was unpredictable at best, that one of skill in the art would have to practice undue experimentation to practice the claimed methods, and that, accordingly, the specification does not teach how to practice gene therapy encompassed by the claims. Applicants respectfully disagree.

Applicants submit that the relevant issue with respect to the enablement of the present claims is whether or not the claims are enabled for **introducing** a nucleic acid molecule into a cell, not whether the claims are enabled for introducing **and** the realization of a biological effect mediated by the introduced biological effector sequence in a gene thereapy setting. That one of skill in the art may practice the present invention in a gene therapy context is not fatal to the enablement of a method for introducing a nucleic acid molecule into a cell.

Applicants submit that they are not required under the law to enable each and every embodiment of the present invention. The Federal Circuit has held that claims may encompass

some inoperative species, so long as the number of inoperative species does not become significant and force one of ordinary skill into undue experimentation in order to practice the invention (*Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 U.S.P.Q. 409 (Fed. Cir. 1984)). As Applicants stated in their previous response of October 8, 2002, the biological effector sequences may be useful for treating specific diseases. The ability of the sequence to treat a disease is a property of the sequence, and not an aspect of the invention which Applicants are required to enable.

Nevertheless, in order to accelerate the prosecution of the present application, Applicants have amended claims 17-19 and 22 to limit the claims to *in vitro* applications of the invention. Applicants submit that, as acknowledged by the Examiner, the claims are enabled for *in vitro* methods, and accordingly request that the rejection be reconsidered and withdrawn.

Rejection of claims 2-22 under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 2-22 under 35 U.S.C. §112, second paragraph for alleged indefiniteness on several grounds.

The Examiner asserts that the claims which were amended in Applicant's response of October 8, 2002 are unclear in lacking antecedent basis for "the molecule of claim 1 or 2" because it is unclear whether the "molecule" refers to the "nucleic acid molecule" or the "cell surface molecule". Applicants submit that the claims have been amended to recite "the nucleic acid molecule of claim...". Applicants therefore request that the rejection be reconsidered and withdrawn.

The Examiner asserts that claims 19, 21, and 22 are indefinite due to confusing syntax. Applicants have made the corrections suggested by the Examiner and therefore request that the rejection be withdrawn.

The Examiner asserts that claims 21 and 22 lack antecedent basis for "said bifunctional molecule...of claim 16". Applicants submit that claim 21 is herein cancelled, and that claim 22 does not recite "said bifunctional molecule...of claim 16". Applicants accordingly request that the rejection be withdrawn.

Rejection of Claims 1, 3, 5, 7, and 16 under 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 3, 5, 7, and 16 under 35 U.S.C. §102(b) as being anticipated by Gold et al. (U.S. Pat. No. 5,270,163). The Examiner asserts that Gold teaches the claimed nucleic acid molecule comprising an aptamer linked to a nucleic acid sequence comprising a biological effector sequence wherein the nucleic acid is DNA or RNA, and wherein a third nucleic acid sequence comprising a different aptamer may be linked or hybridized to the nucleic acid molecule. Applicants respectfully disagree.

Applicants submit that Gold teaches a method of selecting for nucleic acid ligands which can bind to a target molecule. Gold teaches a method of screening and selecting for nucleic acid molecules which can act as ligands and bind to a target molecule based on the secondary or tertiary structure of the nucleic acid. Gold teaches that the nucleic acid sequence can be extended to include the sequence of a second nucleic acid ligand which can bind to a second location on the same target molecule. It appears that it is this teaching which the Examiner is asserting anticipates the molecules of the present invention comprising an aptamer and a biological effector sequence. Gold teaches nucleic acid molecules ligands which can comprise two (or three) nucleic acid ligands which are capable of binding to a target protein via the secondary or tertiary structure of the ligand; each of the nucleic acid ligands of the nucleic acid molecule taught by Gold binds to the same target molecule, albeit at different locations. Applicants submit that the present invention differs from the teachings of Gold in that the bifunctional nucleic acid molecules of Gold comprise two nucleic acid ligands (which if they were to bind to a cell surface molecule, according to the present invention, would be referred to as aptamers), whereas the molecules of the present invention comprise an aptamer (e.g., a nucleic acid ligand which binds to a cell surface molecule; see page 3 of the instant specification) and a biological effector sequence which is not an aptamer (support for the limitation that the biological effector sequence is not an aptamer may be found on page 5, lines 1-5 of Applicant's specification). Thus, unlike Gold, who teaches a nucleic acid molecule comprising two like nucleic acid ligand molecules, the present invention relates to a nucleic acid molecule comprising two disparate components: an aptamer and a biological effector sequence which is

not an aptamer. Accordingly, applicants submit that Gold et al. do not anticipate the claimed invention, and Applicants request that the rejection be reconsidered and withdrawn.

Rejection of Claims 1, 3, 5, 7, 8, 12-14 and 16-18 Under 35 U.S.C. §102(e)

The Examiner has rejected claims 1, 3, 5, 7, 8, 12-14, and 16-18 under 35 U.S.C. §102(e) as being anticipated by Burke et al., in view of Gold et al. (cited only to show that the HIV-1 reverse transcriptase aptamers of Burke are biological effectors). The Examiner asserts that Burke teaches a nucleic acid molecule comprising an aptamer linked to a biological effector sequence. Applicants respectfully disagree.

Applicants submit that Burke teaches the assembly of chimeric nucleic acid molecules including ligands to the HIV-1 reverse transcriptase (col. 15, lines 61-65), chloramphenicol and Coenzyme A (col. 16, lines 49-53), as well as a ribozyme which cleaves near the HIV-1 genome site which binds the tat protein, and an RNA ligand to tat. In contrast, the claims of the present invention relate to a nucleic acid molecule comprising an aptamer and a biological effector sequence wherein the aptamer binds to a cell surface molecule (support may be found on page 6, lines 5-14 of Applicant's specification). There is no teaching in Burke of an aptamer which binds to a cell surface molecule. Accordingly, Applicant submits that Burke et al. does not anticipate the present invention. Applicant therefore requests that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

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